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Low-energy electrons and X-ray irradiation effects on plasma-polymerized allylamine bioactive coatings for stents

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ABSTRACT

Radiation used in biomedical applications causes chemical changes to biomedical materials. This work is an ex situ simulation of the influence of low-energy electron (LEE) impact and X-ray irradiation on the chemical properties of plasma-polymerized allylamine (PPA) bioactive and biocompatible stent coatings. Preliminary X-ray photoelectron spectroscopy (XPS) results show that PPA coatings oxidize in contact with ambient air by the detection of C–O and C=O bonds which are typical of polymer oxidation. Chemical changes after LEE and X-ray irradiation are mainly a loss of oxygen, assuming a surface deoxidizing and not a complete destruction of the surface. XPS survey analyses show that the amine groups remain stable during irradiation. LEE impact measurements by TOF mass spectrometry show that the main ionic losses are H^- ions. It appears that CN groups are stable under irradiation and we observe a loss of hydrogen and oxygen as the main chemical modifications. In conclusion, these results suggest that PPA coatings are stable under biomedical radiation, and they can therefore be used for bioactive and biocompatible stent coatings.

1. Introduction

Stents are used in cardiology to scaffold narrowed arteries so as to reduce the restenosis [1]. Such medical devices are often made of 316 L stainless steel or tantalum. Despite the success of bare metal stents, restenosis remains a major problem after three to six months of implantation [2]. To protect the metallic device from corrosion caused by contact with blood fluid [3] and so to prevent the release of potentially toxic metallic compounds from the corroded stent (e.g. oxides and ions) into the organism [4], it is preferable to coat the stent with an inert material. To this effect, researchers in biomedical engineering have developed a cold plasma polymerization/deposition technique to avoid contact between the blood fluid and the metallic core of the implant. Also, such protection enhances the biocompatibility of the stent and thus reduces the restenosis rate. The improved properties of polymer-coated stents (biocompatibility and blood corrosion resistance) can be accessible by polymerization by cold plasma on the stent surface of C_2F_6 (thus, formation of a fluoropolymer) [5,6] or amino molecules [7]. These kinds of molecule are fully neutral materials for the body and their use is interesting as biocompatible coatings in the biomedical field. The primary amine groups have an additional interest in biomedical coating because of the possibility of chemical grafting of bioactive molecules on the amino sites. These drug-eluting stents are very promising [8–10]. The wet grafting of bioactive molecules on coated-stent surface will allow the dropping of pharmacological molecules as a function of time. These drugs would act as inhibitors of restenosis and could increase the integration of the stent with the arterial wall after implantation. This final stage of surface modification requires a high content of amino functions.

Adequate functioning of the stent is often monitored by successive diagnostic procedures (e.g. X-ray imaging), owning the patient bearing the implant to an increase of exposure to radiation. The large radiation dose absorbed near the implant may become a problem. When X-rays hit a metal surface, secondary low-energy

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electrons (LEEs, at 0–25 eV) are emitted in the surrounding environment with a most probable energy around 2 eV [11]. LEEs are short range particles which interact with biological matter within 1–5 nm [12,13]. Higher energy emitted electrons (e.g. photoelectrons and Auger electrons) has usually a longer penetration depth [13], and therefore do not deposit most of their energy near the surface of the metallic implant. According to our present knowledge, organic molecule or biomolecule lying within 5 nm from a high atomic weight metal surface should experience an increase in radiation damage similar to that found for DNA [11,14]. Consequently radiation damage can alter significantly the chemical structure of the coating, thus its biocompatibility and bioactivity properties. One of our previous works [15] showed that biomedical plasma-fluoropolymer is damaged by X-ray and LEE (0–100 eV) irradiation, principally by loss of fluorine. As the presence of halogen atoms in hydrocarbons has been shown to considerably increase molecular dissociation by 0–10 eV electrons [12], the emission of atomic and ionic fluorine was significant during LEE and X-ray irradiation, showing that the induce damage may deteriorate the coating chemical structure (thus, the properties of biocompatibility) and the bond between the metal and the coating. This situation may be particularly serious in the case of fluorocarbon coatings, since the emission of fluorine during irradiation of a fluoropolymer could be a risk factor for patients after the implantation of fluoropolymer coated stents, depending on the accumulated dose of irradiation received from diagnostic irradiative procedures [15].

On the other hand, the stent coating keeps biological material from being in direct contact with the high radiation dose delivered at the metal surface by LEE during X-ray diagnostic procedures, but the polymer–metal interface becomes more vulnerable to radiation damage. As the properties of biocompatibility and of pharmacological grafting (bioactivity) of plasma-polymerized allylamine (PPA) coating are intrinsically linked to the chemical structure of deposited molecules, alteration of the molecular nature of the coating by biomedical irradiation arising from imaging techniques may cause a loss of desired characteristics owing to the loss of amine groups which allows grafting of pharmacological biomolecules. Biocompatibility can be also reduced by the modification of the nature of the amino layer [16]. This work is thus an ex situ simulation of the influence of imaging techniques on the performance of PPA coated bioactive stents. More specifically, it is a study of the consequences of irradiation on a PPA coating to check if this type of molecules undergoes a significant change of its chemical structure during biomedical imaging. This study focuses on the degradation by X-ray irradiation and LEE impact to simulate the effects of radiation during the use of biomedical radiation techniques.

2. Experimental

2.1. Sample fabrication

316 L stainless steel (Goodfellow, Devon, PA, USA) disks of 12.7 mm of diameter and a thickness of 0.5 mm were punched and were used as substrates to PPA coatings. The protocol for substrate preparation is described in the literature [15]. The disks were electropolished in a solution of 35% phosphoric acid, 50% glycerol and 15% deionised water, at 90 °C for 3 min with a DC current of 1.5 A between the substrate (anode) and a cathode (made of 316 L stainless steel). Thereafter, the disks were rinsed and dried. Finally, the discs were immersed in a solution of hydrofluoric acid (2%), nitric acid (10%) and deionised water (88%) at 50 °C for 30 s, and then rinsed with deionised water and dried. The preparation of substrates was performed at the St-François-d'Assise Hospital (Quebec City, Canada).

The PPA coatings were made at the Laboratoire de Génie des Procédés Plasmas et Traitement de Surface (LGPPTS) at the École Nationale Supérieure de Chimie de Paris (Université de Paris 6, Paris, France). The chemical structure of allylamine is shown in Fig. 1. The coatings were made in a bell-jar type plasma reactor with an asymmetric electrode blade-type configuration, a gas insertion system, a frequency generator (70 kHz), and a pumping system. The plasma reactor setup is fully described in the literature [17,18]. The high voltage electrode, made of stainless steel, is a hollow blade of 20 cm length with a slot opening of 0.5 mm permitting the insertion of gases. The second electrode, which is grounded, is a stainless steel cylinder (diameter: 7 cm; height: 22 cm). During the allylamine coating process, the distance between the electrodes is fixed at 8 mm, and the width of the plasma in contact with the stainless steel substrates is estimated to be 5 mm. A film of low-density polyethylene (LDPE; Goodfellow, thickness of 100 μm) was wrapped around the cylindrical grounded electrode as substrates support. In this configuration, we have treated four samples during each treatment. Before each discharge, the reactor was placed in a vacuum system until a base pressure of about 10^{-3} mbar was reached.

All treatments in the reactor were made in dynamic configuration. Dynamic configuration is equivalent to pulse powered plasma technique [19–21]. The real-processing time (t_{real}), which corresponds to the time during which the plasma interacts with the substrates, is:

$$t_{\text{real}} = t_{\text{exp}}/44. \tag{1}$$

As the speed of rotation of the cylindrical electrode is set at one revolution per second, the minimum t_{real} (corresponding to one round) is 23 ms. This technique limits the fragmentation of the precursor (i.e. the allylamine) by charged particle bombardment or damaging radiation. The polymer coatings thus obtained were more structured and less reticulated than coatings made with continual wave plasma techniques [22]. Choukourov et al. [23] have proposed a polymerization mechanism to account the difference in amine content obtained by continuous wave as compared to pulsed mode plasma polymerization of allylamine. Before the allylamine deposition, the substrates were treated by Ar/H_2 plasma for $t_{\text{exp}} = 20$ min, so $t_{\text{real}} = 27$ s (Eq. (1)). The parameters of this treatment are listed in Table 1. Following the Ar/H_2 treatment, the reactor was purged and the vacuum was restored ($\sim 10^{-3}$ mbar). A mixture of allylamine vapour and argon was inserted in the bell-jar reactor. Deposition parameters were set to make a coating of about 20 nm thick (Table 2) to minimize the possible accumulation of electric charge caused by LEE bombardment. A too thick insulating coating can trap incoming electrons, thus creating a repulsive potential to other incident electrons within energies of interest (0–60 eV) [24]. Insulating layers of the order of 15–20 nm are sufficiently thin to minimize charge accumulation. To avoid the condensation of the allylamine and, at the same time, its degradation during the deposition/polymerization process, the flow tubes, made with stainless steel, that bring the mixture of allylamine/Ar into the bell-jar reactor were heated to 30 °C.

2.2. Sample characterization

The characterization of PPA coatings was performed with a Kratos Axis-Ultra X-ray photoelectron spectroscopy (XPS) system

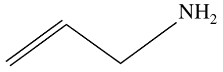

Fig. 1. Chemical structure of allylamine.